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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,120	03/06/2007	**Anil Koul**	GPC0104PUSA	6426

22045 7590 05/11/2009

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EXAMINER	
YOUNG, SHAWQUIA	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
05/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,120	KOUL ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *9-37 and 39-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-43 are currently pending in the instant application. Claims 1-8 and 38 are being rejected and claims 9-37 and 39-43 are withdrawn from consideration in this Office Action.

I. *Priority*

The instant application is a 371 of PCT/EP04/10161, filed on September 10, 2004 which claims benefit of US Provisional Applications 60/502,606, filed on September 15, 2003, 60/551,341, filed on March 10, 2004 and 60/577,043, filed on June 7, 2004 and claims benefit of Foreign Applications EPO 04012814.2, filed May 28, 2004, EPO 03020616.3, filed September 10, 2003 and EPO 04004891.0, filed on March 2, 2004.

Applicants have elected Group IV from the Restriction Requirement which is drawn to a compound of formula (I) wherein Y^1-Y^2-Y^3-Y^4 represents an optionally substituted benzene ring. However, the elected invention is not supported by the following prior-filed applications: US provisional application 60/502,606, filed on September 15, 2003; US provisional application 60/551, 341, filed on March 10, 2004; Foreign Application EPO 03020616.3, filed September 10, 2003 and EPO 04004891.0, filed on March 2, 2004. These prior filed applications disclose compounds wherein Y^1-Y^2-Y^3-Y^4 represents an optionally substituted pyran ring. Thus, Applicants will not receive priority to these applications.

II. *Information Disclosure Statement*

Applicants have not filed an information disclosure statement (IDS) in the instant application.

III. *Restriction/Election*

A. Election: Applicant's Response

Applicants' election without traverse of Group IV in the reply filed on February 19, 2009 is acknowledged.

Subject matter not encompassed by elected Group IV are withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to nonelected inventions.

IV. Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

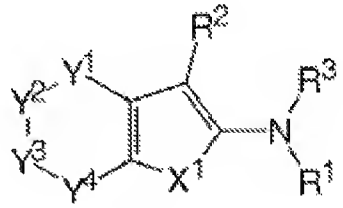
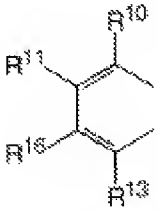
A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

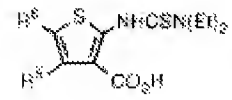
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical

Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

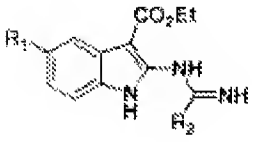
Claims 1 -8 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by *Gutschow, et al.* (J. Med. Chem. 1999); *Showalter, et al.* (J. Med. Chem. 1999); *Bourdais, et al.* (RN 33333-70-9, CAPLUS); *Jagodzinski, et al.* (RN 104053-75-0, CAPLUS); *Ram* (RN 72639-62-4, CAPLUS); *Grinev, et al.* (RN 113407-95-7, CAPLUS); *Kapustina, et al.* (RN 136918-52-0, CAPLUS); *Bridges, et al.* (RN 6433-72-3, CAPLUS); *Shah, et al.* (RN 7311-95-7, CAPLUS); *Hallas, et al.* (RN 92539-88-3, CAPLUS); *Chursinova, et al.* (RN 63673-60-9, CAPLUS); *Callahan, et al.* (RN 633307-96-7, CAPLUS) or *Luk'yanchuk, et al.* (RN 71483-97-1, CAPLUS). The instant elected invention claims a product with the formula  wherein Y^1-Y^2-Y^3-Y^4 is  and all other variables are as defined in claim 1.

The *Gutschow, et al.* reference teaches benzothienyl derivatives such as



wherein R^5 and R^6 form a benzene ring (See compound 49, scheme 4, page 5439). This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Showalter, et al.* reference teaches indole derivatives such as



wherein R_1 is H and R_2 is a methyl or an amine group (See compound 14 c and d, scheme 2, page 5465). This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Bourdais, et al.* reference teaches indole derivatives such as 2-(dimethylamino)-N-phenyl-1H-indole-3-carboxamide which have sedative and antidepressant properties. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Jagodzinski, et al.* reference teaches indole derivatives such as Ethyl ester [3-[(ethylamino)thioxomethyl]-1H-indol-2-yl]-carbamic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Ram* reference teaches benzothienyl derivatives such as Ethyl ester 2-[[(methylamino)thioxomethyl]amino-benzo[b]thiophene-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the

genus structure and its definitions are stated above.

The *Grinev, et al.* reference teaches benzothienyl derivatives such as Ethyl ester 2-(acetylamino)-6-bromo-7-methoxy-benzo[b]thiophene-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Kapustina, et al.* reference teaches benzothienyl derivatives such as Ethyl ester 2-amino-7-hydroxy-6-(phenylthio)-benzo[b]thiophene-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Bridges, et al.* reference teaches indole derivatives such as Ethyl ester 2-amino-1H-indole-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Shah, et al.* reference teaches benzothienyl derivatives such as Ethyl ester 2-amino-benzo[b]thiophene-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Hallas, et al.* reference teaches benzothienyl derivatives such as Methyl ester 2-amino-benzo[b]thiophene-3-carboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Chursinova, et al.* reference teaches indole derivatives such as

Phenylmethyl ester [3-[(phenylamino)carbonyl]-1H-indol-2-yl] carbamic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Callahan, et al.* reference teaches benzothienyl derivatives such as 2-amino-6-(4-fluorophenyl)-benzo[b]thiophene-3-carboxamide. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Luk'yanchuk, et al.* reference teaches benzofuryl derivatives such as Ethyl ester 2-amino-5-hydroxy-4,6, 7-trimethyl-3-benzofuranecarboxylic acid. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered

when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is drawn to a compound of formula (I), as defined in claim 1, for use as a pharmaceutically active agent.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism).

There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute Applicants' claims are drawn to compounds according to claim 1 for use as a pharmaceutically active agent.

Applicants' claim 8 is a broad claim that encompasses the use of the instantly claimed compounds as a pharmaceutically active agent for the treatment of any disease or disorder associated with protein kinase activity. Applicants have disclosed in the specification that the instant compounds can be used in the treatment or prophylaxis of for example, neurodegenerative diseases (i.e. Alzheimer's disease).

Applicants' claims are therefore drawn to a pharmaceutically active agent for the treatment or prophylaxis of Alzheimer's disease. It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by

delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease. (<URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html>.)

In addition, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic agents (*See* e.g., the Cecil Textbood of Medicine, 20th edition (1996), Vol. 2, page 1994).

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the treatment of the diseases encompassed by the broad claim 8.

Test assays and procedure are provided in the specification at pages 179-180 for protein kinase inhibition is generally unpredictable and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are

highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to a compound of formula (I), as defined in claim 1, for use as a pharmaceutically active agent.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all conditions would be benefited by the activity of the claimed compounds and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the

claimed compounds of the invention to be used as a pharmaceutically active agent. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting claim 8.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 is rejected under 35 U.S.C. 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "having the general formula" renders the products indefinite as the phrase "having the general formula" can be considered open-ended language when not clearly defined and therefore is including additional subject matter in the compounds of the formula I that is not described in the instant specification and is not particularly pointed out or distinctly claimed. A claim to a chemical compound cannot be open-ended, but must be claimed with precision. This rejection can be overcome by amending the phrase "having the general formula" to read "of the formula" in claim 1.

V. Objections

Dependent Claim Objections

Dependent Claims 2-58 are also objected to as being dependent upon a rejected based claim. To overcome this objection, Applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim.

VI. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^{c}Kane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/
Examiner, Art Unit 1626
/Rebecca L Anderson/
Primary Examiner, Art Unit 1626